

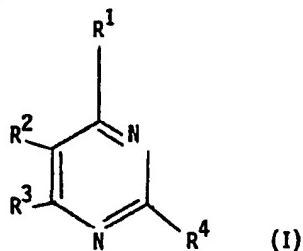
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(54) (2-Fluoroethyl) thio-substituted pyrimidines as nematicides

(57) Compounds of formula (I) are useful as nematicides :



wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, haloalkenyl, alkoxy, alkanoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, CONR⁶R⁷, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, -S(O)_nCH₂CH₂F, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; n is 0, 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄alkyl; R⁵ is C₁₋₄alkyl; provided that at least one of R¹ to R⁴ is -S(O)_nCH₂CH₂F.
Nematicidal compositions and methods of killing or controlling nematodes are also described.

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HETEROCYCLIC COMPOUNDS

The present invention relates to novel pyrimidine derivatives having nematicidal activity, to processes for their preparation, to compositions containing them, and to methods for killing or controlling nematode pests using them.

According to the present invention there is provided a compound of formula (I) wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, haloalkenyl, alkoxy, alkenoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, CONR⁶R⁷, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, -S(O)_nCH₂CH₂F, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; n is 0, 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that at least one of R¹ to R⁴ is -S(O)_nCH₂CH₂F; further provided that when R⁴ is -SCH₂CH₂F, either R¹, R² and R³ are not all hydrogen, or R¹ and R³ are not both methyl when R² is hydrogen.

The compounds of formula (I) in which R⁴ is -SCH₂CH₂F and either R¹, R² and R³ are all hydrogen, or R¹ and R³ are both methyl and R² is hydrogen are known (Khim. Geterotsikl. Soedin 1967 (6), 1087-8). However, their use as nematicides was previously unknown.

When any of R¹ to R⁴ is an alkyl group it can be straight or branched chain and is preferably C₁₋₄ alkyl, in particular ethyl, propyl, isopropyl, n-butyl, iso-butyl, sec-butyl or tertiary butyl.

When any of R¹ to R⁴ is an alkenyl or alkynyl group it can be straight or branched chain and preferably contains up to 6 carbon atoms, for example, allyl or propargyl.

When any of R¹ to R⁴ is a phenyl, phenoxy, benzyl or benzyloxy group, the phenyl moiety may be optionally substituted with halogen, (for example, chlorine, bromine or fluorine), cyano, alkyl, haloalkyl, alkoxy or haloalkoxy, the alkyl group being preferably C₁₋₄ alkyl and the alkoxy group being preferably C₁₋₆ alkyl. Examples of such groups are 2-, 3- or 4-fluorophenyl, 2-, 3- or 4-chlorophenyl, 2,4- or 2,6- difluorophenyl, 2,4- or 2,6- dichlorophenyl, 2-chloro-4-fluorophenyl, 2-chloro-6-fluorophenyl, 2-fluoro-4-chlorophenyl, 2-fluoro-6-chlorophenyl, 2-,3- or 4-methoxyphenyl, 2-, 4-dimethoxyphenyl, 2-, 3-, or 4-ethoxyphenyl, 2-, 3- or 4-methylphenyl,

2-, 3- or 4-ethylphenyl, 2-, 3- or 4-trifluoromethylphenyl, and the corresponding ring substituted benzyl, phenoxy and benzyloxy groups.

When any of R¹ to R⁴ is a cycloalkyl or alkylcycloalkyl group, it preferably contains from 3 to 7 carbon atoms, for example, cyclopropyl, cyclopentyl, cyclohexyl or methylcyclopropyl.

When any of R¹ to R⁴ is halogen, it is preferably fluorine, chlorine or bromine.

When any of R¹ to R⁴ is haloalkyl or haloalkenyl, the halogen is preferably chlorine, fluorine or bromine, the alkyl moiety is preferably C₁₋₄ alkyl, for example trifluoromethyl, trifluoroethyl or pentafluoroethyl, and the alkenyl moiety is preferably C₁₋₆ alkenyl.

When any of R¹ to R⁴ is an alkoxy, alkenoxy or alkoxyalkyl group, it can be straight or branched chain and preferably contains up to 6 carbon atoms, for example, methoxy, ethoxy, propoxy, butoxy, butenoxy, methoxymethyl, methoxyethyl or ethoxymethyl.

When any of R¹ to R⁴ is a haloalkoxy group, it can be straight or branched chain and preferably contains up to 6 carbon atoms. The halogen is preferably chlorine, fluorine or bromine. Particular examples are trifluoromethoxy, trifluoroethoxy or pentafluoroethoxy.

When any of R¹ to R⁴ is a haloalkenoxy group, it can be straight or branched chain and preferably contains up to 6 carbon atoms. The halogen is preferably chlorine, fluorine or bromine. Particular examples are OCH₂CH₂CH=CF₂ and OCH₂CH₂CH=CHF.

When any of R¹ to R⁴ is an alkylthio group, the alkyl preferably contains up to 4 carbon atoms. For example, -S-methyl, -S-ethyl, -S-propyl, S-butyl.

When any of R¹ to R⁴ is a haloalkylthio group, the alkyl preferably contains up to 4 carbon atoms, for example, methyl, ethyl, propyl, butyl. The halogen is preferably chlorine, fluorine or bromine. Particular examples are SCF₃, -S(CH₂)₂CH₂F, SCH₂CH₂F, SCBrF₂, SCClF₂ and SCH₂CF₃.

When any of R¹ to R⁴ is -S(O)_nCH₂CH₂F is is preferably a substituent in the R¹ or R⁴ position, or alternatively, in both the R¹ and R⁴ positions or in both the R¹ and R³ positions.

When any of R¹ to R⁴ is NR⁵R⁶, it is preferably NHCH₃, N(CH₃)₂ or N(C₂H₅)₂.

When any of R¹ to R⁴ is acylamino, it is preferably NHCOCH₃ or NCOC₂H₅.

When any of R¹ to R⁴ is CO₂R⁷, R⁷ is preferably hydrogen, methyl or ethyl.

When any of R¹ to R⁴ is O(CH₂)_mCO₂R⁷, m is preferably 2 and R⁷ is preferably hydrogen, methyl or ethyl.

When any of R¹ to R⁴ is CONR⁶R⁷, R⁶ and R⁷ are preferably hydrogen, methyl or ethyl. Especially preferred is CONH₂.

When R² and R³ are taken together to form a 5- or 6-membered ring, it is preferably a carbocyclic ring, for example, -(CH₂)₃-, -(CH₂)₄- or -CH=CH-CH=CH-.

Of particular interest are the compounds of formula (I) where R¹ is selected from C₁₋₄ alkyl, C₁₋₄ haloalkyl, halogen, C₁₋₆ alkoxy or hydroxy, R² is selected from hydrogen or C₁₋₄ alkyl, R³ is selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₆ alkoxy, hydroxy or halogen and R⁴ is S(O)_nCH₂CH₂F where n is 0. Or alternately, the compounds of formula (I) where R¹ is phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted, R² is hydrogen or C₁₋₄ alkyl, R³ is selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₆ alkoxy, hydroxy or halogen and R⁴ is S(O)_nCH₂CH₂F where n is 0.

Also of particular interest are the compounds of formula (I) where R¹ is S(O)_nCH₂CH₂F where n is 0, R² is selected from hydrogen and C₁₋₄ alkyl, R³ is selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, hydroxy or halogen and R⁴ is selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, halogen, C₁₋₆ alkoxy or hydroxy. Or alternately, the compounds of formula (I) where R¹ is S(O)_nCH₂CH₂F, R² is hydrogen or C₁₋₄ alkyl, R³ is selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₆ alkoxy, hydroxy or halogen and R⁴ is selected from phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted.

Examples of the compounds of formula (I) are set out in Table I.

TABLE I

COMPOUND NO.	R ¹	R ²	R ³	R ⁴
1	H	H	H	SCH ₂ CH ₂ F
2	CH ₃	H	H	SCH ₂ CH ₂ F
3	SCH ₂ CH ₂ F	H	H	H
4	SCH ₂ CH ₂ F	H	H	SCH ₂ CH ₂ F
5	OCH ₂ CF ₃	H	H	SCH ₂ CH ₂ F
6	SCH ₂ CH ₂ F	H	SCH ₂ CH ₂ F	H
7	OCH ₃	H	n-C ₃ H ₇	SCH ₂ CH ₂ F
8	OC ₅ H ₁₁	H	H	SCH ₂ CH ₂ F
9	OC ₄ H ₉	H	H	SCH ₂ CH ₂ F
10	OCH ₂ CH=CHCH ₃	H	H	SCH ₂ CH ₂ F
11	OH	H	n-C ₃ H ₇	SCH ₂ CH ₂ F
12	CF ₃	H	H	SCH ₂ CH ₂ F
13	SCH ₂ CH ₂ F	H	O(CH ₂) ₂ C ₂ F ₅	H
14	SCH ₂ CH ₂ F	H	OCH ₂ CF ₃	H
15	Cl	H	n-C ₃ H ₇	SCH ₂ CH ₂ F
16	OCH ₂ C ₆ H ₅	H	H	SCH ₂ CH ₂ F
17	OCH ₂ CO ₂ CH ₃	H	H	SCH ₂ CH ₂ F
18	n-C ₃ H ₇	H	H	SCH ₂ CH ₂ F
19	OCH ₂ (4-Cl-C ₆ H ₄)	H	H	SCH ₂ CH ₂ F
20	C ₆ H ₅	H	OCH ₂ CH ₃	SCH ₂ CH ₂ F
21	OH	H	CH(CH ₃) ₂	SCH ₂ CH ₂ F
22	Cl	H	CH(CH ₃) ₂	SCH ₂ CH ₂ F
23	O(CH ₂) ₂ CO ₂ CH ₃	H	H	SCH ₂ CH ₂ F
24	OCH ₃	H	CH(CH ₃) ₂	SCH ₂ CH ₂ F
25	CH(CH ₃) ₂	H	H	SCH ₂ CH ₂ F
26	OH	-(CH ₂) ₄ -		SCH ₂ CH ₂ F
27	OCH ₃	-(CH ₂) ₄ -		SCH ₂ CH ₂ F
28	Cl	-(CH ₂) ₄ -		SCH ₂ CH ₂ F
29	CH ₃	H	H	SCH ₂ CH ₂ F
30	H	C(CH ₃) ₃	H	SCH ₂ CH ₂ F
31	H	C ₂ H ₅	H	SCH ₂ CH ₂ F
32	H	CF ₃	H	SCH ₂ CH ₂ F
33	H	CH(CH ₃) ₂	H	SCH ₂ CH ₂ F

TABLE I continued

COMPOUND NO.	R ¹	R ²	R ³	R ⁴
34	H	Cl	H	SCH ₂ CH ₂ F
35	H	C ₆ H ₅	H	SCH ₂ CH ₂ F
36	H	-(CH ₂) ₃ -		SCH ₂ CH ₂ F
37	H	-(CH ₂) ₃ -		SCH ₂ CH ₂ F
38	H	-(CH ₂) ₃ -		SCH ₂ CH ₂ F
39	CH ₃	CH ₃	CH ₃	SCH ₂ CH ₂ F
40	CH ₃	CH ₃	CH ₃	SCH ₂ CH ₂ F
41	-C≡CH	H	H	SCH ₂ CH ₂ F
42	CN	H	H	SCH ₂ CH ₂ F
43	4-F-C ₆ H ₄	H	H	SCH ₂ CH ₂ F
44	4-F-C ₆ H ₄	H	H	SCH ₂ CH ₂ F
45	4-CF ₃ -C ₆ H ₄ CH ₂	H	H	SCH ₂ CH ₂ F
46	C ₆ H ₅	H	H	SCH ₂ CH ₂ F
47	1-CH ₃ -C ₃ H ₅	H	H	SCH ₂ CH ₂ F
48	CH ₂ CF ₃	H	H	SCH ₂ CH ₂ F
49	OCH ₂ CF ₃	H	Cl	SCH ₂ CH ₂ F
50	CH ₂ OCH ₃	H	H	SCH ₂ CH ₂ F
51	Cl	H	Cl	SCH ₂ CH ₂ F
52	F	H	F	SCH ₂ CH ₂ F
53	F	H	H	SCH ₂ CH ₂ F
54	SCH ₃	H	F	SCH ₂ CH ₂ F
55	C(CH ₃) ₃	H	H	S(O)CH ₂ CH ₂ F
56	C(CH ₃) ₃	H	OCH ₂ CH ₃	SCH ₂ CH ₂ F
57	H	-CH=CH-CH=CH-		SCH ₂ CH ₂ F
58	H	-CH=CH-CH=CH-		SCH ₂ CH ₂ F
59	H	-CH=CH-CH=CH-		SCH ₂ CH ₂ F
60	OCH ₂ CF ₃		-CH=CH-CH=CH-	SCH ₂ CH ₂ F
61	OCH ₂ CF ₃	H	H	S(O) ₂ CH ₂ CH ₂ F

^c indicates the substituent is cyclic

The compounds of formula (I) where R¹ to R⁴ have the meanings defined above and n is 0 are prepared by reacting a correspondingly substituted mercaptopyrimidine of formula (I) where one or both of R¹ and R⁴ is SH, with 1-bromo-2-fluoroethane in the presence of a base such as a carbonate,

for example, potassium carbonate, and an inert solvent, for example acetone. Both the mercaptopyrimidine and 1-bromo-2-fluoroethane can be obtained by conventional methods or from commercial sources.

Thus, according to a further aspect of the present invention there is provided a process for the preparation of compounds of formula (I) where R¹ to R⁴ have the meanings defined above which comprises reacting a correspondingly substituted compound of formula (I) where one or both of R¹ and R⁴ is SH, with 1-bromo-2-fluoroethane in the presence of a base.

A particularly useful method of preparing the 4-mercaptopyrimidine comprises reacting the corresponding 4-hydroxypyrimidine in a solvent containing a tertiary amine, (e.g. pyridine) with phosphorous pentasulphide under a nitrogen atmosphere.

The compounds of formula (I) where any one or more of R¹ to R⁴ is alkoxy can alternatively be prepared by reacting the corresponding hydroxy derivative of formula (I) with an alkylating agent, for example, dimethyl sulphate.

Thus, according to a further aspect of the present invention there is provided a process for the preparation of compounds of formula (I) where R¹ to R⁴ have the meanings defined above provided that at least one of R¹ to R⁴ is alkoxy, which comprises reacting a corresponding hydroxy derivative of formula (I) with an alkylating agent.

The compounds of formula (I) where R¹ to R⁴ have the meanings defined above and n is 1, are prepared by oxidising the correspondingly substituted compound of formula (I) when n is 0, using conventional methods, for example by treatment with a peroxide in an inert organic solvent. The compounds of formula (I) where R¹ to R⁴ have the meanings defined above and n is 2, are prepared by oxidising the correspondingly substituted compound of formula (I) where n is 0 or 1 using conventional method, for example, by treatment with a peroxide in an inert organic solvent.

Suitable peroxides include organic peroxides such as peroxy carboxylic acids, or their salts, for example, magnesium monoperoxy-phthalic acid. Suitable inorganic peroxides include potassium peroxymono-sulphate.

Thus, according to a further aspect of the present invention there is provided a process for the preparation of compounds of formula (I) where n is 1 and R¹ to R⁴ have the meanings defined above, which comprises reacting a correspondingly substituted compound of formula (I) when n is 0 with an oxidising agent; and a process for the preparation of compounds of formula (I) where n is 2 and R¹ to R⁴ have the meanings defined above, which

comprises reacting a correspondingly substituted compound of formula (I) when n is 0 or 1 with an oxidising agent.

The compounds of formula (I) are nematicidal and can be used to control nematodes in crop plants. Therefore, in a further aspect of the invention, there is provided a method for killing or controlling nematodes which comprises applying to the locus of the pests or to a plant susceptible to attack by the pest an effective amount of a compound of formula (I) wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, haloalkenyl, alkoxy, alkenoxy, alkoxalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, amino, NR⁵R⁶, CONR⁶R⁷, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, -S(O)_nCH₂CH₂F, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; n is 0, 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that at least one of R¹ to R⁴ is -S(O)_nCH₂CH₂F.

The term "controlling" extends to non-lethal effects which result in the prevention of damage to the host plant and the limitation of nematode population increase. These effects may be the result of chemical induced disorientation, immobilisation, or hatch prevention or induction. The chemical treatment may also have deleterious effects on nematode development or reproduction.

The compounds of the invention can be used against both plant-parasitic nematodes and nematodes living freely in the soil. Examples of plant-parasitic nematodes are: ectoparasites, for example Xiphinema spp., Longidorus spp. and Trichodorus spp.; semi-endoparasites, for example, Tylenchulus spp.; migratory endoparasites, for example, Pratylenchus spp., Radopholus spp. and Scutellonema spp.; sedentary endoparasites, for example, Heterodera spp., Globodera spp. and Meloidogyne spp.; and stem and leaf endoparasites, for example, Ditylenchus spp., Aphelenchoïdes spp. and Hirshmaniella spp..

The compounds of the invention can also be used in combating a range of insects and acarids. Examples include Lepidoptera, Diptera, Homoptera and Coleoptera (including *Diabrotica* i.e. corn rootworms).

In order to apply the compound to the locus of the nematode or to a plant susceptible to attack by the nematode, the compound is usually formulated into a composition which includes in addition to the compound of

formula (I) suitable inert diluent or carrier materials, and/or surface active agents. Thus in a further aspect of the invention there is provided a nematicidal composition comprising an effective amount of a compound of formula (I) wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, haloalkenyl, alkoxy, alkenoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, CONR⁶R⁷, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, -S(O)_nCH₂CH₂F, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; n is 0, 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that at least one of R¹ to R⁴ is -S(O)_nCH₂CH₂F; and an inert diluent or carrier material and optionally a surface active agent.

The amount of composition generally applied gives a rate of active ingredient from 0.01 to 10 kg per hectare, preferably from 0.1 to 6 kg per hectare.

The compositions can be applied to the soil, plant or seed, in the form of dusting powders, wettable powders, granules (slow or fast release), emulsion or suspension concentrates, liquid solutions, emulsions, seed dressings, fogging/smoke formulations or controlled release compositions, such as microencapsulated granules or suspensions.

Dusting powders are formulated by mixing the active ingredient with one or more finely divided solid carriers and/or diluents, for example natural clays, kaolin, pyrophyllite, bentonite, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium phosphates, calcium and magnesium carbonates, sulphur, lime, flours, talc and other organic and inorganic solid carriers.

Granules are formed either by absorbing the active ingredient in a porous granular material for example pumice, attapulgite clays, fuller's earth, kieselguhr, diatomaceous earths, ground corn cobs, and the like, or on to hard core materials such as sands, silicates, mineral carbonates, sulphates, phosphates, or the like. Agents which are commonly used to aid in impregnation, binding or coating the solid carriers include aliphatic and aromatic petroleum solvents, alcohols, polyvinyl acetates, polyvinyl alcohols, ethers, ketones, esters, dextrins, sugars and vegetable oils. with the active ingredient. Other additives may also be included, such as emulsifying agents, wetting agents or dispersing agents.

Microencapsulated formulations (microcapsule suspensions CS) or other controlled release formulations may also be used, particularly for slow release over a period of time, and for seed treatment.

Alternatively the compositions may be in the form of liquid preparations to be used as dips, irrigation additives or sprays, which are generally aqueous dispersions or emulsions of the active ingredient in the presence of one or more known wetting agents, dispersing agents or emulsifying agents (surface active agents). The compositions which are to be used in the form of aqueous dispersions or emulsions are generally supplied in the form of an emulsifiable concentrate (EC) or a suspension concentrate (SC) containing a high proportion of the active ingredient or ingredients. An EC is a homogeneous liquid composition, usually containing the active ingredient dissolved in a substantially non-volatile organic solvent. An SC is a fine particle size dispersion of solid active ingredient in water. To apply the concentrates they are diluted in water and are usually applied by means of a spray to the area to be treated.

Suitable liquid solvents for ECs include methyl ketone, methyl isobutyl ketone, cyclohexanone, xylenes, toluene, chlorobenzene, paraffins, kerosene, white oil, alcohols, (for example, butanol), methylnaphthalene, trimethylbenzene, trichloroethylene, N-methyl-2-pyrrolidone and tetrahydrofurfuryl alcohol (THFA).

Wetting agents, dispersing agents and emulsifying agents may be of the cationic, anionic or non-ionic type. Suitable agents of the cationic type include, for example, quaternary ammonium compounds, for example cetyltrimethyl ammonium bromide. Suitable agents of the anionic type include, for example, soaps, salts of aliphatic monoesters of sulphuric acid, for example sodium lauryl sulphate, salts of sulphonated aromatic compounds, for example sodium dodecylbenzenesulphonate, sodium, calcium or ammonium lignosulphonate, or butylnaphthalene sulphonate, and a mixture of the sodium salts of diisopropyl- and triisopropynaphthalene sulphonates. Suitable agents of the non-ionic type include, for example, the condensation products of ethylene oxide with fatty alcohols such as oleyl alcohol or cetyl alcohol, or with alkyl phenols such as octyl phenol, nonyl phenol and octyl cresol. Other non-ionic agents are the partial esters derived from long chain fatty acids and hexitol anhydrides, the condensation products of the said partial esters with ethylene oxide, and the lecithins.

These concentrates are often required to withstand storage for prolonged periods and after such storage, to be capable of dilution with water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. The concentrates may contain 10-85% by weight of the active ingredient or ingredients. When diluted to form aqueous preparations such preparations may contain varying amounts of the active ingredient depending upon the purpose for which they are to be used.

The compounds of formula (I) may also be formulated as powders (dry seed treatment DS or water dispersible powder WS) or liquids (flowable concentrate FS, liquid seed treatment LS, or microcapsule suspension CS) for use in seed treatments. In use the compositions are applied to the nematodes, to the locus of the nematodes, to the habitat of the nematodes, or to growing plants liable to infestation by the nematodes, by any of the known means of applying pesticidal compositions, for example, by dusting, spraying, or incorporation of granules.

The compounds of the invention may be the sole active ingredient of the composition or they may be admixed with one or more additional active ingredients such as nematicides or agents which modify the behaviour of nematodes such as hatching factors, insecticides, synergists, herbicides, fungicides or plant growth regulators where appropriate.

Suitable additional active ingredients for inclusion in admixture with the compounds of the invention may be compounds which will broaden the spectrum of activity of the compounds of the invention or increase their persistence in the location of the pest. They may synergise the activity of the compound of the invention or complement the activity for example by increasing the speed of effect or overcoming repellency. Additionally multi-component mixtures of this type may help to overcome or prevent the development of resistance to individual components.

The particular additional active ingredient included will depend upon the intended utility of the mixture and the type of complementary action required. Examples of suitable insecticides include the following:

- a) Pyrethroids such as permethrin, esfenvalerate, deltamethrin, cyhalothrin in particular lambda-cyhalothrin, biphenthin, fenpropathrin, cyfluthrin, tefluthrin, fish safe pyrethroids for example ethofenprox, natural pyrethrin, tetramethrin, s-bioallethrin, fenfluthrin, prallethrin and 5-benzyl-3-furylmethyl-(E)-(1R,3S)-2,2-dimethyl-3-(2-oxothiolan-3-ylidenemethyl) cyclopropane carboxylate;

- b) Organophosphates such as profenofos, sulprofos, methyl parathion, azinphos-methyl, demeton-s-methyl, heptenophos, thiometon, fenamiphos, monocrotophos, profenophos, triazophos, methamidophos, dimethoate, phosphamidon, malathion, chloropyrifos, phosalone, terbufos, fensulfothion, fonofos, phorate, phoxim, pyrimiphos-methyl, pyrimiphos-ethyl, fenitrothion or diazinon;
- c) Carbamates (including aryl carbamates) such as pirimicarb, cloethocarb, carbofuran, furathiocarb, ethiofencarb, aldicarb, thiofurox, carbosulfan, bendiocarb, fenobucarb, propoxur or oxamyl;
- d) Benzoyl ureas such as triflumuron, or chlorofluazuron;
- e) Organic tin compounds such as cyhexatin, fenbutatin oxide, azocyclotin;
- f) Macrolides such as avermectins or milbemycins, for example such as abamectin, avermectin, and milbemycin;
- g) Hormones and pheromones;
- h) Organochlorine compounds such as benzene hexachloride, DDT, chlordane or dieldrin;
- i) Amidines, such as chlordimeform or amitraz;
- j) Fumigant agents.

In addition to the major chemical classes of insecticide listed above, other insecticides having particular targets may be employed in the mixture if appropriate for the intended utility of the mixture. For instance selective insecticides for particular crops, for example stemborer specific insecticides for use in rice such as cartap or buprofezin can be employed. Alternatively insecticides specific for particular insect species/stages for example ovo-larvicides such as chlofentezine, flubenzimine, hexythiazox and tetradifon, moltilicides such as dicofol or propargite, acaricides such as bromopropylate, chlorobenzilate, or growth regulators such as hydramethylon, cyromazin, methoprene, chlorofluazuron and diflubenzuron may also be included in the compositions.

Examples of suitable synergists for use in the compositions include piperonyl butoxide, sesamax, safroxan and dodecyl imidazole.

Suitable herbicides, fungicides and plant-growth regulators for inclusion in the compositions will depend upon the intended target and the effect required.

An example of a rice selective herbicides which can be included is propanil, an example of a plant growth regulator for use in cotton is "Pix", and examples of fungicides for use in rice include blasticides such as blasticidin-S. The ratio of the compound of the invention to the other

active ingredient in the composition will depend upon a number of factors including type of target, effect required from the mixture etc. However in general, the additional active ingredient of the composition will be applied at about the rate as it is usually employed, or at a slightly lower rate if synergism occurs.

The following Examples illustrate the invention. The compounds were identified and characterised by means of the melting points, nuclear magnetic resonance spectroscopy (^1H NMR δ (CDCl_3)), infra red (IR) or mass spectroscopy (M^+).

EXAMPLE 1

This example illustrates the preparation of Compound No. 1 of Table I.

1-Bromo-2-fluoroethane (1.135g) was added dropwise to a stirred mixture of 2-mercaptopurine (0.987g) and potassium carbonate (1.246g) in acetone (20ml) at room temperature. The mixture was heated under reflux for 2 hours and then left to stand overnight at room temperature.

The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with water and brine, dried with magnesium sulphate and evaporated under reduced pressure to give 2-(2-fluoroethylthio)-purine as a yellow liquid :

Compound No. 1

NMR : 8.55 (2H,d); 7.01 (1H,t); 4.75, 4.59 (2H,2xt); 3.52, 3.45 (2H,2xt)
 M^+ : 158, 112

EXAMPLE 2

This example illustrates the preparation of Compound No. 2 of Table I.

1-Bromo-2-fluoroethane (0.561g) was added dropwise to a stirred mixture of 2-mercaptopurine hydrochloride (0.653g) and potassium carbonate (1.089g) in acetone (15ml) at room temperature. The mixture was heated under reflux for 2 hours and then left to cool to room temperature.

The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with water and brine, dried with magnesium sulphate and evaporated under reduced pressure to give 2-(2-fluoroethylthio)-4-methylpurine as a brown liquid :

Compound No. 2

NMR : 8.37 (1H,d); 6.86 (1H,d); 4.76, 4.58 (2H,2xt); 3.51, 3.45 (2H,2xt);
2.46 (3H,s)
 M^+ : 172, 151

EXAMPLE 3

This example illustrates the preparation of Compound No. 3 of Table I.

(a) Preparation of 4-mercaptopurine

To a stirred suspension of 4-hydroxypyrimidine (100g) in dry pyridine (500ml) at room temperature under nitrogen was added phosphorus pentasulphide (100g) in a single portion. An exotherm to 54°C was noted. The mixture was allowed to cool to room temperature and stirred at that temperature for 30 minutes prior to heating at 96°C (steam bath) for 1 hour.

The mixture was cooled to room temperature and poured into water (1000ml) and concentrated to dryness. The residue was triturated with water (200ml) and the brown solid collected by filtration and washed with water (200ml).

Recrystallisation from water and drying under vacuum over P_2O_5 gave 4-mercaptopurine (84.34g, 72%) as orange needles. The product was used without further purification.

(b) Preparation of Compound No. 3 of Table I.

1-Bromo-2-fluoroethane (0.548g) was added dropwise to a stirred mixture of 4-mercaptopurine (0.442g) and potassium carbonate (0.567g) in acetone (10ml) at room temperature. The mixture was heated under reflux for 2 hours and then left to stand overnight at room temperature.

The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with water and brine, dried with magnesium sulphate and evaporated under reduced pressure to give 4-(2-fluoroethylthio)-pyrimidine as a brown liquid :

Compound No. 3

NMR : 8.94 (1H,s); 8.35 (1H,d); 7.20 (1H,d); 4.75, 4.57 (2H,2xt); 3.68,
3.49 (2H,2xt)

M^+ : 158, 137

EXAMPLE 4

This Example illustrates the preparation of Compound No. 4 of Table I.

1-Bromo-2-fluoroethane (1.15g) was added dropwise to a stirred suspension of dithiouracil (0.569g) and potassium carbonate (1.14g) in acetone (15ml) at room temperature. The mixture was heated under reflux for 2.5 hours and then allowed to stand at room temperature overnight.

The reaction mixture was quenched with water and extracted with ethyl acetate. The organic phase was washed with water and brine, dried using magnesium carbonate and evaporated under reduced pressure to give

2,4,-bis(2-fluoroethylthio)-pyrimidine as a brown liquid.

NMR : 8.15 (1H,d); 6.89 (1H,d); 4.74 (2H,m); 4.57 (2H,m); 3.58-3.37 (4H,m)

M⁺ : 236, 28

IR : 1545s, 1410s (film).

EXAMPLE 5

In order to illustrate the nematicidal properties of the compounds of formula (I), compounds from Table I were tested on root knot nematodes and cyst nematodes.

Methodology

Cucumber plants (9 days old, variety 'Telegraph') were soil drenched with a composition of a compound of formula (I) (obtained by diluting 1 part of a solution of the compound in a 1:1 mixture of acetone and ethanol with 99 parts of water containing 0.05% of a wetting agent) at a rate of 40ppm in a drench volume of 10ml/45g of soil. The plants were infested with second stage juveniles of the root knot nematode Meloidogyne incognita after the solution of the compound had been absorbed by the soil. Nematodes were applied to the roots in a solution of water. The roots of the plants were examined after 9 days to determine the percentage reduction in the number of root knots compared with a control treatment omitting the compound. There were 3 replicates per treatment.

TABLE II

COMPOUND NO.	% ROOT KNOT REDUCTION AT 40 PPM
1	51
2	62
3	68
4	99

The compounds of the invention not only display nematicidal activity, a further advantage is that the compounds are not phytotoxic to the target plant. Very little phytotoxicity was observed in the above tests. This is a particularly desirable feature when treating young plants and seeds.

The following examples demonstrate formulations suitable for applying the compounds of the present invention. The amount of ingredient is expressed in parts by weight or grams per litre as indicated. A * indicates a trademark.

EXAMPLE 5

This example demonstrates granules suitable for soil application. The granules can be made by standard techniques such as impregnation, coating, extrusion or agglomeration.

	<u>Zw/w</u>
Impregnated granule : Active ingredient	5
Wood Rosin	2.5
Gypsum granules (20-40 mesh)	92.5
Coated granule : Active ingredient	0.5
'Solvesso' * 200	0.4
Calcium carbonate granules (30-60 mesh)	99.1
Slow release granule : Active ingredient	10
Polyvinylacetate/vinyl chloride copolymer latex	5
Attapulgus granules	85

EXAMPLE 6

This example demonstrates formulations for use as a spray. The compounds can be formulated as wettable powders, water dispersible granules, suspension concentrates, emulsifiable concentrates, emulsions or microcapsule suspensions for application diluted in water.

	<u>g/l</u>
Emulsifiable concentrate: Active ingredient	250
Calcium dodecyl-	50
benzene sulphonate	
Nonyl phenol ethoxylate	50
Alkylbenzene solvent	to 1 litre
	<u>Zw/w</u>
Wettable powder : Liquid active ingredient	40
lignosulphonate dispersant	5
silica	25
sodium lauryl sulphate	3
china clay (kaolin)	27
Microcapsule suspension : Liquid active ingredient	250
toluene diisocyanate	10
polymethylene polyphenyl isocyanate	20

nonyl phenol ethoxylate	6
lignosulphonate dispersant	15
xanthan gum	1
bentonite	10
biocide 'Proxel'*	0.1
sodium carbonate	5
water	to 1 litre

The microcapsule suspensions can be used as a spray, soil drench or as an intermediate to prepare slow release granules for application to the soil.

Suspension concentrate :	<u>g/l</u>
Solid active ingredient	400
lignosulphonate dispersant	50
sodium lauryl sulphate	30
xanthan gum	1
biocide 'Proxel'*	0.1
bentonite	10
water	to 1 litre

EXAMPLE 7

This example demonstrates formulations suitable for use as seed treatments in conventional application machinery.

Dry seed treatment	<u>Zw/w</u>
: Active ingredient	20
dodecyl benzene	3
Rubine Toner (dyestuff)	2.7
Talc	53.3
Silica	to 100%

The suspension concentrate and microcapsule suspension of Example 6 can be used as flowable concentrates for seed treatment.

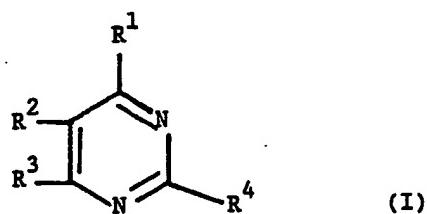
EXAMPLE 8

This example demonstrates the formulation of the compounds for electrostatic spraying.

	<u>g/l</u>
Active ingredient	200
N-methylpyrrolidone	50
Soyabean oil	120
'Solvesso' 200	to 1 litre

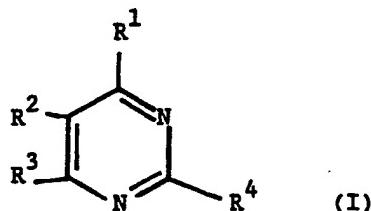
CHEMICAL FORMULAE

(corresponding to formulae numbers in description)



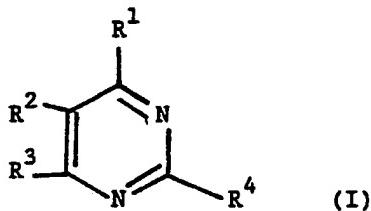
CLAIMS

1. A compound of formula (I) :



wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, haloalkenyl, alkoxy, alkenoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, CONR⁶R⁷, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, -S(O)_nCH₂CH₂F, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; n is 0, 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that at least one of R¹ to R⁴ is -S(O)_nCH₂CH₂F; further provided that when R⁴ is -SCH₂CH₂F, either R¹, R² and R³ are not all hydrogen, or R¹ and R³ are not both methyl when R² is hydrogen.

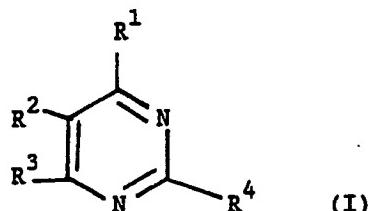
2. A nematicidal composition comprising an effective amount of a compound of formula (I) :



wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, alkoxy, alkenoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that one or both of R¹ and R⁴ is -S(O)_nCH₂CH₂F wherein

n is 0, 1 or 2; and an inert diluent or carrier material and optionally a surface active agent.

3. A method for killing or controlling nematode pests which comprises applying to the locus of the pests or to a plant susceptible to attack by the pest an effective amount of a compound of formula (I) :



wherein R¹, R², R³ and R⁴ are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkylcycloalkyl, halogen, haloalkyl, alkoxy, alkenoxy, alkoxyalkyl, haloalkoxy, haloalkenoxy, alkylthio, haloalkylthio, cyano, nitro, amino, NR⁵R⁶, hydroxy, acylamino, -CO₂R⁷, -O(CH₂)_mCO₂R⁷, phenyl, phenoxy, benzyl or benzyloxy, the phenyl group or phenyl moiety of the benzyl group being optionally substituted in the ring; or R² and R³ when taken together form a 5- or 6-membered ring; m is 1 or 2; R⁶ and R⁷ are hydrogen or C₁₋₄ alkyl; R⁵ is C₁₋₄ alkyl; provided that one or both of R¹ and R⁴ is -S(O)_nCH₂CH₂F where n is 0, 1 or 2.

4. Process for the preparation of the compounds of formula (I) as defined in any of claims 1 to 3 which comprises reacting a corresponding substituted compound of formula (I) where one or both of R¹ and R⁴ is SH with 1-bromo-2-fluoroethane in the presence of a base.
5. Process for the preparation of compounds of formula (I) according to claim 4 in which R¹ is -SCH₂CH₂F which comprises reacting the correspondingly substituted 4-mercaptopurine with phosphorous pentasulphide in a tertiary amine solvent and under a nitrogen atmosphere.

Patents Act 1977
Examiner's report to the Comptroller under Section 17
(The Search report)

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Application number
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Relevant Technical Fields		Search Examiner S J QUICK
(i) UK Cl (Ed.M)	C2C (CQL, CQM, CQS, CRQ)	
(ii) Int Cl (Ed.5)	C07D 239/00	Date of completion of Search 29 SEPTEMBER 1994
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X	Chem. Abstr., Vol 70, no 4015 and Izv. Akad. Nauk SSSR, Ser. Khim., 1968, Vol (8), pages 1841-1846, see abstract (especially highlighted sentence).	1 and 4
X	Chem. Abstr., Vol 69, no 67316 and Khim. Geterotsikl. Soedin., 1967, Vol (6), pages 1087-1088, see online record (especially title); acknowledged in this application.	4
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